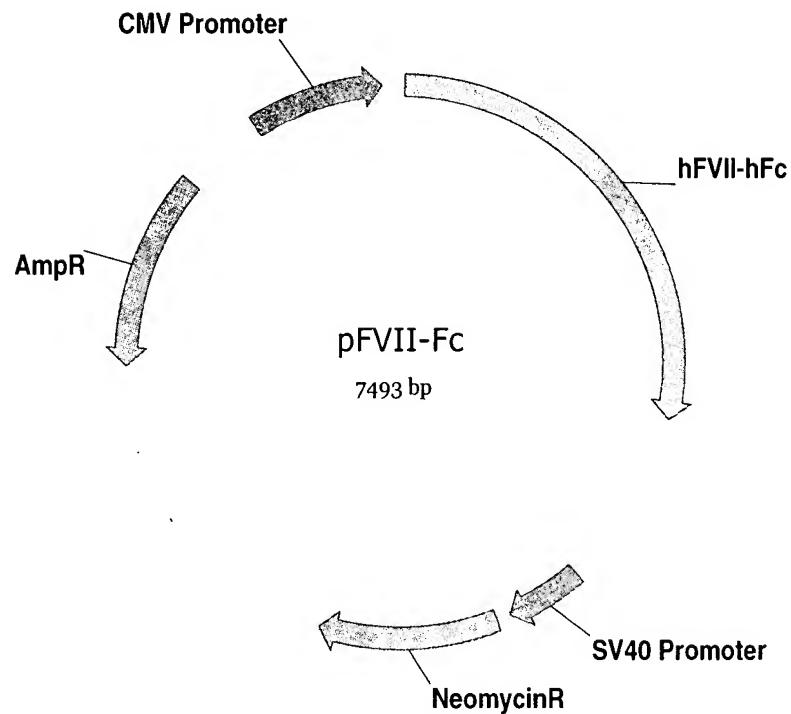


FIGURE 1 – Plasmid vector pFVII-Fc according to example 1

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FIGURE 2

SEQ ID NO:1 (The amino acid sequence of native human coagulation Factor VII):

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Ala-Asn-Ala-Phe-Leu-GLA-GLA-Leu-Arg-Pro-Gly-Ser-Leu-GLA-Arg-GLA-Cys-Lys-

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GLA-GLA-Gln-Cys-Ser-Phe-GLA-GLA-Ala-Arg-GLA-Ile-Phe-Lys-Asp-Ala-GLA-Arg-

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Thr-Lys-Leu-Phe-Trp-Ile-Ser-Tyr-Ser-Asp-Gly-Asp-Gln-Cys-Ala-Ser-Ser-Pro-

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Cys-Gln-Asn-Gly-Gly-Ser-Cys-Lys-Asp-Gln-Leu-Gln-Ser-Tyr-Ile-Cys-Phe-Cys-

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Leu-Pro-Ala-Phe-Glu-Gly-Arg-Asn-Cys-Glu-Thr-His-Lys-Asp-Asp-Gln-Leu-Ile-

75

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90

20

Cys-Val-Asn-Glu-Asn-Gly-Gly-Cys-Glu-Gln-Tyr-Cys-Ser-Asp-His-Thr-Gly-Thr-

95

100

105

Lys-Arg-Ser-Cys-Arg-Cys-His-Glu-Gly-Tyr-Ser-Leu-Leu-Ala-Asp-Gly-Val-Ser-

25

110

115

120

125

Cys-Thr-Pro-Thr-Val-Glu-Tyr-Pro-Cys-Gly-Lys-Ile-Pro-Ile-Leu-Glu-Lys-Arg-

130

135

140

30

Asn-Ala-Ser-Lys-Pro-Gln-Gly-Arg-Ile-Val-Gly-Gly-Lys-Val-Cys-Pro-Lys-Gly-

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160

Glu-Cys-Pro-Trp-Gln-Val-Leu-Leu-Val-Asn-Gly-Ala-Gln-Leu-Cys-Gly-Gly-

165

170

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180

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Thr-Leu-Ile-Asn-Thr-Ile-Trp-Val-Val-Ser-Ala-Ala-His-Cys-Phe-Asp-Lys-Ile-

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Lys-Asn-Trp-Arg-Asn-Leu-Ile-Ala-Val-Leu-Gly-Glu-His-Asp-Leu-Ser-Glu-His-
200 205 210 215

5 Asp-Gly-Asp-Glu-Gln-Ser-Arg-Arg-Val-Ala-Gln-Val-Ile-Ile-Pro-Ser-Thr-Tyr-
220 225 230

Val-Pro-Gly-Thr-Thr-Asn-His-Asp-Ile-Ala-Leu-Leu-Arg-Leu-His-Gln-Pro-Val-
235 240 245 250

10 Val-Leu-Thr-Asp-His-Val-Val-Pro-Leu-Cys-Leu-Pro-Glu-Arg-Thr-Phe-Ser-Glu-
255 260 265 270

Arg-Thr-Leu-Ala-Phe-Val-Arg-Phe-Ser-Leu-Val-Ser-Gly-Trp-Gly-Gln-Leu-Leu-
15 275 280 285

Asp-Arg-Gly-Ala-Thr-Ala-Leu-Glu-Leu-Met-Val-Leu-Asn-Val-Pro-Arg-Leu-Met-
290 295 300 305 306

20 Thr-Gln-Asp-Cys-Leu-Gln-Gln-Ser-Arg-Lys-Val-Gly-Asp-Ser-Pro-Asn-Ile-Thr-
310 315 320

Glu-Tyr-Met-Phe-Cys-Ala-Gly-Tyr-Ser-Asp-Gly-Ser-Lys-Asp-Ser-Cys-Lys-Gly-
325 330 335 340

25 Asp-Ser-Gly-Gly-Pro-His-Ala-Thr-His-Tyr-Arg-Gly-Thr-Trp-Tyr-Leu-Thr-Gly-
345 350 355 360

Ile-Val-Ser-Trp-Gly-Gln-Gly-Cys-Ala-Thr-Val-Gly-His-Phe-Gly-Val-Tyr-Thr-
30 365 370 375

Arg-Val-Ser-Gln-Tyr-Ile-Glu-Trp-Leu-Gln-Lys-Leu-Met-Arg-Ser-Glu-Pro-Arg-
380 385 390 395

35 Pro-Gly-Val-Leu-Leu-Arg-Ala-Pro-Phe-Pro
400 405 406

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SEQ ID NO:2 (DNA primer 1 for preparation of hFVII-hFc):

5'- GCTAGCCACCATGGTCTCCCAGGCCCTCAG -3' (SEQ ID NO:2)

5 SEQ ID NO:3 (DNA primer 2 for preparation of hFVII-hFc):

5'- CGAGCCCCATTCCCGGATCCGCAGAGCCCAAATCTTGT -3' (SEQ ID NO:3)

SEQ ID NO:4 (DNA primer 3 for preparation of hFVII-hFc):

5'- CGAGCCCCATTCCCGGATCCGCAGAGCCCAAATCTTGT -3' (SEQ ID NO:4)

10

SEQ ID NO:5 (DNA primer 4 for preparation of hFVII-hFc):

5'- TTGCCGGCCGTCGCACTCATTAA -3' (SEQ ID NO:5)

15 SEQ ID NO:6 (The amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide (underlined) conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined. :

MVSQALRLCLLGLQQCLAAGGVAKASGGETRDMPWKGPHRVFVTQEEAHGVLR~~RRR~~RANAF
LEELRPGSLERECKEEQCSFEEAREIFKDAERTKLFWISYSDGDQCASSPCQNGSCKDQLQSYICF

20 CLPAFEGRNCETHKDDQLICVNENGGCEQYCS
DHTGTRSCRCHEGYSLADGVSCTPTVEYPCGKI
PILEKRKNASKPQGRIVGGKVC
PKGECPWQVLLVNGAQLCGGT
LINTIWVVAHCFDKIKNWRNLIA
VLGEHDLSEHDGDEQSRRVAQV
IIPSTYVPGTTNHDIALLRLHQP
VVLTDHVVP
LCLPERTF
SERTLAF
VRFSLVSGWGQQLDRGATA
LELMVNV
PRLMTQDCLQQ
SRKVGDS
PNITEY
MFCAGY
SDGS
KDSC
K
GDSGGPHATHYRG
TWYLTGIV
SWGQGCAT
VGHFGV
YTRVSQY
IEWLQ
KLMRSE
PRPG
VLLRAP
PP
25 GSAEPKSCDKTHTC
CPPCPAPELLGGPSVFL
FPPKPKDTLM
ISRTPEV
TCVV
DVS
HEDPEV
KF
FN
WY
V
DGVEVHNA
KT
KP
REE
QY
NSTY
RV
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S
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SEQ ID NO:7 (Amino acid sequence of Fc domain from IgG1):

EPKSCDKTHTC
CPPCPAPELLGGPSVFL
FPPKPKDTLM
ISRTPEV
TCVV
DVS
HEDPEV
KF
FN
WY
V
EVHNA
KT
KP
REE
QY
NSTY
RV
V
S
V
L
T
V
L
H
QD
W
L
N
G
K
C
K
V
S
N
K
A
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P
A
I
E
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T
I
S
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A
G
Q
P
R
E
P
Q
V
Y

35

TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

5

SEQ ID NO:8 (The amino acid sequence of native human coagulation Factor VII conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined, X refers to GLA residues):

10 ANAFLXXLRPGSLRXCKXQCSFXXARXIFKDAXRTKLFWISYSDGDQCASSPCQNGGSCKDQLQS
YICFCLPAFEGRNCETHKDDQLICVNENGGCEQYCSDDHTGTRSCRCHEGYSLLADGVSCPTVEYP
CGKIPILEKRNASKPQGRIVGGKVCVKGECPWQVLLVNGAQLCGGTLINTIWWVSAAHCFDKIKNWR
NLIAVLGEHDLSEHDGDEQSRRVAQVIIPSTYVPGTTNHDIALLRLHQPVVLTDHVVPLCLPERTFSER
TLAFVRFLVSGWGQLLDRGATALELMVNVPRLMTQDCLQQSRKVGDSPNITEYMFCAGYSDGSK
15 DSCKGDSGGPHATHYRGTWYLGTIVSWGQGCATVGHFGVYTRVSQYIEWLQKLMRSEPRPGVLLR
APFPGSAEPKSCDKTHTCPPCPAPELLGGPSVFLPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

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SEQ ID NO:9 (cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide conjugated to Fc domain of IgG1):

atggctcccaggccctcaggctccctgccttgcgtggcgtcaggcgtgcaggcgggtcgtaaggccctcaggaggagaaa
cacgggacatgccgtggaaaggccggggccctcacaaggacttcgtcgtaaccaggagaaggccacggcgctctgcacccggccggccgc
25 aacgcgttccgtggaggagactgcggccgggtccctggagggaggatgtcaaggaggaggactgtccctcgaggaggccggggagatcttc
aaggacgcggagaggacgaactgttctggattttacagtgtatggggaccatgtgcctcaagtccatgcagaatggggctctgcaag
gaccagctccagtcataatctgttctgcctccctgcctcgaggccggaaactgtgagacgcacaaggatgaccagctgtatgtgaacg
agaacggccgtgtgagcgtactgcgtgaccacacgggacccaagcgtccctgtcggtccacgagggtactctgtctggcagacgg
30 ggtgtctgcacaccacacagtgtaatatccatgtggaaaaatacctattctgaaaaaaatggggatccatgtccaccccaaggccaaatgtgg
ggggcaagggtgtccccaaaggggatgtccatggcgggtctgttggtaatggagactcgtgtgtgggggacccgtatcacacca
tctgggtgtctccgcggccactgttgcacaaaatcaagaactggaggaaacctgtcgccgtgtggcgagcacgacctcagcgagcac
gacggggatgagcagacggccgggggtggcgcaggatgtcatcccccacgtacgtccggccacccacgcacatcgccgtct
ccgcctgcaccagccctggctctactgaccatgtgtggccctctgcctggcggaaacggacgttctctgagaggacgtggcccttcgtcgct
40 ttcatttgtcagcggctggggccacgtgtggaccgtggccacggccctggaggtctatgtgtcaacgtgtcccggtatgaccagg
actgcctgcacgcgtacggaaagggtggagactcccaaataatcacggagtacatgttctgtggccgtactcggatggcagcaaggact
gcccggggacagtggaggcccacatgccacccactaccggggcactgtgttgcacccatgtcgccgtgtggccggctgccc
accgtggggcacttgggggtgtacaccagggtctccctgtccatgtcgatgtggccctgtccatgtcgccgtgtggccggctgccc
ctgcggagcccaattccggatccgcagagcccaaactctgtgacaaaactcacacatgccaccgtggccacgtggccctgtatc
accgtcaatgttctctcccccaaaaacccaaggacaccctcatgtatccggggacccctgtggatgtggccgtgtggccggatgt
gaagaccctgggtcaagtcaacttgtacgtggacggcgtggagggtgtcataatgccaagacaaaagccggggaggagcgtacaacag
cacgtaccgtgtggcagcgtccaccgtccctgcaccaggactggctgtcaatggcaaggagtacaagtgcacagggtacaccctg
cagcccccacatcgagaaaaccatctcaaagccaaaggccagcccgagaaccacacagggtacaccctgccccatccggatgt
accaagaaccaggcgtacgcctgaccctgtcaaggctctatcccagcgtacatgcggcgtggagtgccggagacatggcagccgag

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aacaactacaagaccacgcgtcccggtctggactccgcacggctcttccttccatcagcaagcgtaccgggtggacaagagcaggllggcagca
ggggaaacgcgtcttcatgtccgtgtgcgtggactccgcacggctcttccttccatcagcaagcgtaccgggtggacaagagcaggllggcagca

5 SEQ ID NO:10 (cDNA sequence encoding the vector comprising the cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide conjugated to Fc domain of IgG1:

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SEQ ID NO:11 (The amino acid sequence of native human coagulation Factor VII with propeptide (underlined) conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined. Construct is made according to example 1):

40 **MVSQALRLCLLLGLQGCLAAVFVTQEEAHGVLHRRRRAAFLEELRPGSLERECKEEQCSFEAR**
 EIFKDAERTKLFWISYSDGDQCASSPCQNGGSKDQLQSYICFLPAFEGRNCETHKDDQLICVNEN
 GGCEQYCSDDHTGKRSRCHEGYSLADGVSCTPTVEYPCGKIPILEKRNASKPQGRIVGGKVCPKG
 ECPWQVLLVNGAQLCGGTINTIWVSAAHCFDKIKNWRNLIAVLGEHDLSEHDGDEQSRRVAQVII
 45 **PSTYVPGTTNHDIALLRLHQPVVTDHVVPCLPERTFSERTLA** FVRFSLVSGWGQLLDRGATALELM
 VLNVPRLMTQDCLQQSRKVGDSPNITEYMFCAGYSDGSKDSCKGDSGGPHATHYRGTWYLTGIVS
 WGQQCATVGHFGVYTRVSQYIEWLQKLMRSEPRPGVLLRAPFFGSAEPKSCDKTHTCPCPAPELL
 GGPSVFLFPPKPKDLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTPREEQNSTYRV
 VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK
 50 **GFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHY**
 TQKSI SLSPGK

SEQ ID NO:12 (cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with propeptide conjugated to Fc domain of IgG1, cDNA construct is made according to example 1):

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25 SEQ ID NO:13 (cDNA sequence encoding the vector comprising the cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with propeptide conjugated to Fc domain of IgG1, cDNA construct is made according to example 1):

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